REMARKS

The Final Office Action of June 18, 2009, has been carefully reviewed. The claims are amended above to address objections in the Final Action and to incorporate the subject matter of claim 16 into each of claims 10, 11 and 18, and the claims resulting from the amendments above are claims 10, 11, 18, 20 and 21. Applicants again believe and respectfully but resolutely submit that the claims define novel and unobvious subject matter and therefore should be allowed. Favorable reconsideration, entry of the amendments presented above, and allowance are earnestly solicited.

Applicants believe and respectfully submit that no new issues are presented because the independent claims now incorporate the features of claim 16 which has been previously considered by the Examiner.

Acknowledgment by the PTO of the receipt of Applicants' papers filed under §119 is noted.

Regarding the objections to claims 10, 11 and 18, the spelling of the word granulocyte is corrected above. G-CSF is now presented without parentheses.

On the other hand, the word "therefor" is correct. It is an adverb which basically means "for that". In other words, the effective amount called for in claim 18 is "there" (i.e. is present) "for" repairing/regenerating renal tissue in a state of nephropathy. On the other hand, the word "therefore" is a conjunction which means "consequently".

Withdrawal of the objections is in order and is respectfully requested.

Claims 22 and 23 have been rejected under the second paragraph of §112 as being unclear. The rejection is respectfully traversed.

The meaning of claims 22 and 23 is explained in the short paragraph at the bottom of page 5 of the last reply. These claims were presented to emphasize or "more clearly specify that the effective dosage is based on the G-CSF itself, …." However, on further reflection, Applicants agree with the Examiner that these claims are unnecessary and perhaps even redundant, and so they have been deleted without prejudice, with the understanding of Applicants that the Examiner already interprets the effective amount in claims 10 and 11 to be the effective amount of the G-CSF.

Claims 10, 20 and 21 have been finally rejected as anticipated by Shishido, previously applied. This rejection is respectfully traversed for the reasons of record, respectfully repeated by reference, and for the additional reasons given below.

Claim 10, and thus claims 20 and 21 as well, call for a method for proliferating or regenerating renal tissue or a cell present in renal tissue, wherein the renal tissue is in a state of diabetic nephropathy. This is simply not disclosed by Shishido.

The position of the Examiner as expressed in the Final Action is based on alleged inherency as asserted as follows:

> *The therapeutic agent's properties are inherent to its function and the activity of the agent does not stop because the use was not an intended use. Once the G-CSF is administered to a nephropathic patient, the drug would exert its action irrespective to the etiology of the disease.*

Respectfully, this misses the point. Claim 10 is not directed to G-CSF itself, and is not directed to the application of G-CSF to

any and all types of renal tissue, but instead is directed to a method for proliferating or regenerating renal tissue or a cell present in renal tissue when the renal tissue is in a state of diabetic nephropathy. Shishido does not disclose administration of G-CSF to a diabetic nephropathic patient. There is no inherency and there is no anticipation because Shishido does not disclose what is claimed.

For a reference to be properly anticipatory under §102, the reference must disclose each and every element of the claimed invention, *Eli Lilly and Co. v. Zenith Goldline Pharms., Inc.*, 81 USPQ2d 1324, 1328 (Fed. Cir. 2006), and those elements must be "arranged or combined in the same way as in the claim," *Net MoneyIN Inc. v. VeriSign Inc.*, 88 USPQ2d 1751, 1759 (Fed. Cir. 2008), quoting from *Finisar Corp. v. DirecTV Group Inc.*, 86 USPQ2d 1609, 1618 (Fed. Cir. 2008). Shishido clearly does not meet the test for anticipation.

Attached please find a partial translation of Shishido. As is described in the Shishido abstract, rhG-CSF promotes production and release of neutrophil from bone marrow, and it enhances neutrophil function. Shishido describes on page 97 that "rhG-CSF is partially metabolized in the liver, but the kidneys are the main organs for its excretion. Thus, this study was conducted for the purpose of clarifying the pharmacokinetics, effects and safety of rhG-CSF in renal failure patients."

Shishido discloses that rhG-CSF can be administered safely to the patients with renal failure, namely rhG-CSF can exert its function of promoting production and releasing neutrophil without serious side effects. Shishido neither discloses nor teaches that rhG-CSF is effective in the treatment of renal disease.

The function of promoting production and releasing neutrophil as disclosed by Shishido is entirely irrelevant to proliferating or regenerating renal tissue or a cell present in renal tissue. Thus the use is entirely different. According to the examiner's logic, any second method of use of a drug cannot be allowed, but this is clearly not correct.

Shishido and two other references were cited in the International Search Report as "A" category documents, which category defines the general state of the art which is not considered to be of particular relevance. Actually, the International Preliminary Examination Report states as follows:

"The invention set forth in claims 1 to 9 is not disclosed in any of the documents cited in the international search report, and is therefore novel and involves an inventive step.

"In particular, documents 1 to 3 neither disclose nor suggest that G-CSF promotes the repair and regeneration of kidney tissue, and is effective in the treatment of renal failure."

Applicants of course understand that the Examiner is not bound either by the International Search Report designation of the "A" category of Shishido or the International Preliminary Examination Report (IPER). Nevertheless, the facts support the categorization of Shishido as a "A" reference (general state of the art only) and the comments of the IPER. Moreover, the PTO, as a matter of comity and harmonization, should not brush aside or ignore what occurred during the international phase without good reason, and there is certainly no good reason in the present situation for the Examiner to have done so. Attached is a copy of the IPER which confirms what is stated above.

Applicants wish to briefly return to the issue of alleged inherency. Recalling, as pointed out on pages 6 and 7 of the preceding Reply, that Shishido can only be considered at <u>most</u> to

refer to a generic problem (renal failure) which comprises many species, but does not disclose the use of G-CSF in conjunction with the claimed species, if follows that there is no reasonable certainty that inherency exists as regards the claimed species. For inherency to be applicable in a rejection under §102, the inherency must be reasonably certain. Please see *In re Robertson*, 49 USPQ2d 1949, 1951 (Fed. Cir. 1999):

> Inherency, however, may not be established by probabilities or possibilities. The mere fact that a certain thing may result from a given set of circumstances is not sufficient. [citations omitted]

Also see *In re Oelrich*, 212 USPQ 323, 326 (CCPA 1981), stating that the inherency of a feature in a reference must be inevitable, not merely possible or even probable.

"Absent a showing [by the PTO] of some reasonable certainty of inherency, the rejection... under 35 USC §102 must fail." *In re Brink*, 164 USPQ 247, 249. Again, as there is no reasonable certainty that Shishido ever treated a patient with diabetic nephropathy, it follows that inherency cannot be assumed and does not legally exist.

Withdrawal of the rejection is in order and is respectfully requested.

Claims 10 and 20-23 have been rejected under §102 as anticipated by Fukuda. This rejection is again respectfully traversed for the reasons set forth in the preceding reply, respectfully repeated by reference, and for the additional reasons pointed out below.

Fukuda relates to a method for treating ischemic disease comprising administering G-CSF and HGF. In paragraph [0017],

Fukuda mentions various ischemic diseases including ischemic renal disease. The present claims have been amended to specify diabetic nephropathy. Fukuda does not disclose or teach that G-CSF itself is effective in proliferating or regenerating renal tissue or a cell present in renal tissue in a state of diabetic nephropathy.

The points raised in the above remarks against the rejection based on Shishido apply equally to the rejection based on Fukuda, and these remarks are respectfully repeated by reference. Fukuda does not explicitly disclose what is claimed, and Fukuda does not inherently provide what is claimed. Therefore, Fukuda does not anticipate any of Applicants' claims.

Withdrawal of the rejection is in order and is respectfully requested.

Claims 11 and 16-18 have been rejected as obvious under §103 from Shishido in view of newly applied Shi et al U.S. Application Publication 2002/0012966 (Shi), and also as obvious under §103 from Fukuda in view of Shi.[1] These rejections are respectfully traversed.

The deficiencies as regards the present invention of Shishido and Fukuda have been pointed out above and previously. Shi has not been cited to make up for those deficiencies, and indeed does not do so. Therefore, even if the proposed combinations were obvious, the resultant reconstructed primary references would not reach claims 11 and 18 (claim 16 having been incorporated into claims 11 and 18, and claim 17 having been

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[1] Applicants do not see where Shi has been officially cited of record, and requests the Examiner to point out where it has been cited. If it has not been cited so far, Applicants request that the Examiner cite Shi officially of record on a Form PTO-892.

deleted without prejudice to Applicants' rights to pursue the subject matter of claim 17 at a later time, without any penalty whatsoever, Applicants in such a case relying on §§120 and 119).

In more detail, and as stated above, neither Shishido nor Fukuda discloses or suggests that G-CSF promotes the repair and regeneration of renal tissue, or is even effective in the treatment of renal failure as claimed. More particularly, both Shishido and Fukuda are entirely silent concerning the treatment of diabetic nephropathy.

Shi relates to novel human secreted proteins and at most includes a huge basket or shotgun disclosure of possible uses, which leads the person of ordinary skill in the art to nothing in particular. Paragraph [0644] merely mentions a large number of kidney diseases including diabetic nephropathy, but does not disclose that the proteins can be used in the treatment of any of these diseases, or how they might be used for any such diseases. In particular, Shi does not disclose or teach that G-CSF is effective in the treatment of the kidney diseases. The examiner asserts that some of the proteins may be used to treat diabetic nephropathy, and that the proteins can be used in conjunction with growth factors such as G-CSF, but who knows?

Because Shishido and Fukuda are entirely silent about the treatment of diabetic nephropathy, the person of ordinary skill in the art would have had no reason to even try to use G-CSF in the treatment of diabetic nephropathy even upon consideration of the disclosure of Shi along with the disclosures of Shishido and Fukuda. Applicants believe and respectfully submit that the prior art provides no reason why one would even want to combine the references or teach how they might be combined if one wanted to do so.

To summarize, (1) the proposed combinations would not reach the claimed subject matter even if the combinations were obvious, (2) the proposed combinations would not have been obvious for the reasons pointed out above, and (3) the prior art provides no reasonable expectation of achieving Applicants' results.

Withdrawal of the rejections is in order and is respectfully requested.

Favorable reconsideration, entry of the Amendments presented above, and allowance are respectfully urged.

Respectfully submitted,

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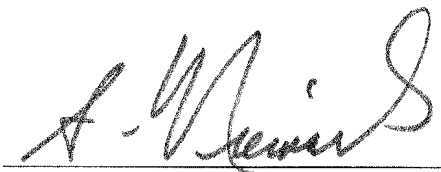
By 
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